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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/020,095 | 12/14/2001 | D. Wade Walke | LEX-0282-USA | 9959 |
| 24231 | 7590 | 09/02/2004 | EXAMINER | |
| LEXICON GENETICS INCORPORATED 8800 TECHNOLOGY FOREST PLACE THE WOODLANDS, TX 77381-1160 | | | SCHNIZER, HOLLY G | |
| | | | ART UNIT | PAPER NUMBER |
| | | | 1653 | |

DATE MAILED: 09/02/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/020,095

Applicant(s)

WALKE ET AL.

Examiner

Holly Schnizer

Art Unit

1653

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
 - If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
 - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
 - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 07 June 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-3 and 5-7 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☐ Claim(s) 1-3 and 5-7 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

Art Unit: 1653

DETAILED ACTION

Status of the Claims

The Response and Amendment filed June 7, 2004 has been entered and considered. Claim 4 has been cancelled and Claims 5-7 have been added. Therefore, Claims 1-4 and 5-7 are pending and have been considered on the merits in this Office Action.

Election/Restrictions

Applicant's confirmation of the election without traverse of Group I in the reply filed on June 7, 2004 is acknowledged. Thus, the restriction requirement is FINAL.

Rejections Withdrawn

The rejection of Claim 2 under 35 U.S.C. 112, first paragraph as failing to comply with the written description requirement is withdrawn since the claim requires that the cDNA molecule encodes the amino acid sequence shown in SEQ ID NO:4.

Rejections Maintained

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Art Unit: 1653

Claims 1-3, and new Claims 5-6 are rejected under 35 U.S.C. 101, for reasons of record, set forth in the office action mailed January 28, 2004, pages 4-8, because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

Applicants' arguments have been addressed below.

Applicants first argue that sequence identity between the claimed polynucleotides and those known at the time of filing the present application has nothing to do with the standard for patentability under 35 U.S.C. 101. The examiner notes that this comparison of the claimed polynucleotide sequences with sequences known at the time of filing the present application was to establish whether or not the claimed polynucleotide had any well-established utility at the time of filing the present Application. As stated in the previous office action, it appears that, at the time of filing, there was no well-established utility for the claimed polynucleotides. Applicants have provided sequences that have 98% identity at the amino acid level over the entire length of SEQ ID NO:3 in Exhibit B. Applicants contend that the availability of these sequences at the time of filing is irrelevant to the determination of patentability under 35 U.S.C 101. However, the sequences of Exhibit B published in 2002 and 2004, well after the filing date of the present invention, do not provide evidence of what the skilled artisan understood at the time of filing the present application.

Applicants argue that the instant invention has a number of substantial and credible utilities, not the least of which is in forensic analysis. Applicants point out that

Art Unit: 1653

the use of the presently described polymorphisms in forensic analysis does not require the identification of a specific medical condition, but to distinguish individual members of the human population based on the presence or absence of one or both of the described polymorphisms. In the worst case scenario, each marker is useful to distinguish 50% of the population, thus, the ability to eliminate 50% of the population from a forensic analysis is clearly a real world, practical utility.

This argument has been considered but is not deemed persuasive. First, using the claimed nucleic acids to distinguish individual members of the human population based on the presence or absence of one of the described polymorphisms does not afford the claimed nucleic acids specific and substantial utility, because Applicants have not disclosed the significance of the presence of the claimed nucleic acid in a subject. The mere presence or absence of the claimed nucleic acid in a subject is not substantial utility, because any DNA can be used for said general purpose. In order for the presently claimed nucleic acid to be considered as having specific and substantial utility in forensic analysis, it must provide significant information about an individual, other than that it is either present or absent in said individual. Thus, using the claimed DNA to identify or rule out criminal suspects or to identify human remains or in paternity determination is not considered specific and substantial because any polymorphism could be used for these purposes. There is no doubt that SNP research is a significant and emerging field. For example, the presence of a specific SNP can be used to identify those individuals who are likely to benefit from a new medication, from those who could suffer adverse side effects or to determine the optimal dosage. However, in the instant

Art Unit: 1653

case, Applicants have not shown that the claimed nucleic acid can be used in any meaningful way, other than that it may distinguish 50% of the population as having it. Does this mean that those individuals that have it: are susceptible to certain diseases, are unique and can be solely identified because of the presence of said DNA?

Applicants also argue that the claimed sequences share 98% identity with a sequence that has been annotated as CD109 and that CD109 has a known activity of expressing the Gov alloantigen system, which has been associated with neonatal alloimmune thrombocytopenia, platelet transfusion refractoriness, and post-transfusion purpura. Applicants refer to Exhibit D for abstracts (Solomon et al. that they contend support their argument. Applicants further argue that since the function of CD109 is known, the present situation exactly tracks Example 10 of the Revised Interim Utility Guidelines Training Materials.

This argument has been considered but is not deemed persuasive. The Specification teaches that the sequences of the present invention share structural similarity with animal macroglobulin proteins and other animal proteins including but not limited to complement proteins and cytochrome oxidase (p. 2, lines 1-4). The Specification does not teach that the cDNAs of the present invention encode CD109 and there is no evidence that a CD109 with similarity to the claimed sequences was known at the time of filing. Thus, it appears that at the time of filing, one of skill in the art would have only understood that the claimed cDNAs encoded proteins that had similarity to the alpha macroglobulin family of proteins. However, as evidenced by the full length article of the abstract cited in Exhibit C (Solomon et al., Gene 327: 171-183,

Art Unit: 1653

2004), the alpha macroglobulin family includes many members, such as alpha 2 macroglobulin, pregnancy zone protein, complement proteins C3, C5, KIAA1283, and CD109, that have distinct roles and functions in the innate immune system (see Solomon et al., p. 171, Col. 1). Where a class of proteins is defined by common structural features, but evidence shows that the members of the class do not share a specific and substantial functional utility, membership in the class may not impute a specific and substantial utility to the new member of the class (see Revised Utility Guidelines; Fed. Reg. Vol. 66, NO. 4, pp. 1092-1099 at p. 1096, Col. 3, second paragraph). Thus, the present case differs from example 10 of the Training materials because in example 10 the sequence claimed had similarity to a ligase. A ligase is well known in the art to ligate DNA and thus has a common substrate (DNA) and performs a common task (to ligate DNA). On the contrary, all members of the alpha macroglobulin family would not have the same utility as evidenced in Solomon et al. Thus, the assertion in the specification that the claimed polynucleotides encoded a protein that had some structural similarity to alpha macroglobulin proteins would not apprise the skilled artisan of how to use that protein since various members of the alpha macroglobulin family have different functions and utilities.

Applicants further argue that if each and every invention were required to have a unique utility, the Patent and Trademark office would no longer be issuing patents on batteries, automobiles, golf balls and treatments of a variety of diseases. Furthermore, if a composition needed to be unique to be patented, the entire class and subclass system would be an effort in futility, as the class and subclass system serves solely to

Art Unit: 1653

group such common inventions. Applicants cite *In re Brana*, 34 USPQ2d 11436 (Fed. Cir. 1995) and contend that "the Office is confusing the requirements under the law for obtaining a patent with the requirements for obtaining government approval to market a particular drug for human consumption". Applicants argue even if further research might be required in certain aspects of the instant invention, this does not preclude a finding that the invention has utility, because courts have stated that "pharmaceutical inventions, necessarily includes the expectation of further research and development". However, the need for some experimentation does not render the claimed invention unpatentable. Applicants further submit that it has been clearly established that a statement of utility in a specification must be accepted absent reasons why one skilled in the art would have a reason to doubt the objective truth of such statement.

This argument is unpersuasive because while each and every composition does not have to be unique in order for it to be patented, it has to have a specific and substantial utility. And, as stated in the previous office action (p. 4, line3-4) because a specific and substantial utility has not been found, credibility has not been assessed. The skilled artisan must know how to use said composition. Novel golf balls, automobiles and batteries must provide a useful improvement over already existing golf balls, automobiles and batteries, in order to satisfy the requirements under 35 U.S.C. § 101. The need for further research does not necessarily equate the lack of utility, however, in the instant case, Applicants have not provided one single specific and substantial utility for the claimed nucleic acid, other than general uses that are applicable to all DNAs. *In re Brana*, 34 USPQ 1436, 1441 (Fed. Cir. 1995), disclosed

Art Unit: 1653

compounds with specific structure and specific activity. Thus, in that case evidence of success in structurally similar compounds was relevant in determining whether one skilled in the art would believe an asserted utility; therefore, an implicit assertion of a tumor target was sufficiently specific to satisfy the threshold utility requirement.

Furthermore, in re Brana, there were test results showing that several compounds within the scope of the claims exhibited significant antitumor activity against standard tumor model in vivo. However, instant Applicants do not provide an activity for the proteins encoded by the claimed nucleic acid, nor do they provide the physiological significance of these proteins, only, an assertion that the proteins of the instant application can be used in forensic analysis. Thus, because the application lacks any specific and substantial utility, credibility cannot be assessed.

Applicants argue that the Examiner's response to the Applicants argument that the claimed nucleic acid could be used in high through-put DNA chips, is flawed, because firstly, expression profiling does not require a knowledge of the function of the particular nucleic acid on the chip, rather the gene chip indicates which DNA fragments are expressed at greater or lesser levels of two or more particular tissue types. Second, the particular cell types and controls in which the expression levels are assessed directly indicate to the skilled artisan whether "the polynucleotide expression should be increased or decreased". Also, the skilled artisan already have used and continue to use sequences such as Applicants in gene chip applications every day, without any information about the polynucleotide or the encoded protein. It defies logic that skilled artisan would waste money and time by including such sequences on gene chips if they

Art Unit: 1653

did not yield any useful information. Furthermore, Applicants contend that only the assertion of one credible utility is needed to meet the requirement of under 35 U.S.C. § 101.

This argument is not considered persuasive. Although the knowledge of the function of a particular nucleic acid may not be necessary for said nucleic acid to be used in a gene chip, the significance of the altered levels or forms of a gene in a tissue compared to another tissue must be known. Furthermore, Applicants' have not disclosed those conditions or reasons in which it might be desirable to increase or decrease the claimed nucleic acid. Therefore, following the expression levels of a nucleic acid without the knowledge of the conditions and circumstances that would lead the skilled artisan to increase or decrease it, would be meaningless. Finally, evidence of commercial success, while sometimes persuasive as secondary evidence of non-obviousness, is immaterial to utility and enablement. Many products have enjoyed commercial success due to fads or clever advertising, wherein the products would not have met the legal standards for utility and enablement.

Applicants also argue that another specific utility for the claimed nucleic acids is in "identification of coding sequence" and "mapping a unique gene to a particular chromosome". Applicants argue that the claimed nucleic acids have utility not because they can be used to produce the encoded protein, but because they provide biologically validated empirical data, that specifically define that portion of the corresponding genomic locus that actually encodes exon sequence. Also, significant is the claimed sequences define how encoded exons are actually spliced together to produce active

Art Unit: 1653

transcripts. Thus Applicants submit that the practical scientific value of biologically validated, expressed, spliced and polyadenylated mRNA sequences is readily apparent to those skilled in the art. Applicants also argue that the claimed nucleic acids provide specificity in localizing the specific region of human chromosome 6 that contains the gene encoding the given polynucleotide, a utility not shared by virtually any other nucleic acid sequences. Applicants state that Venter et al demonstrates the significance of expressed sequence information in the structural analysis of genomic data.

This argument is not considered persuasive. Using the claimed polynucleotide as a chromosomal marker is not considered a specific utility because no meaningful information will be obtained from tracking the level of expression of the claimed polynucleotide because there is no physiological or biological significance attached to these nucleotides or the encoded proteins. Without a disclosure of a particular disease state in which the claimed nucleic acid are expressed at an altered level or form, it would be impossible to determine what the results of a gene expression monitoring assay mean. For example, if a compound is tested on a microarray comprising the claimed nucleic acid and affects expression of the nucleic acid negatively, it cannot be determined if that means that the compound is a potential good drug for a disease or would exacerbate the disease if administered. The test results also would not have meaning in terms of what specific disease is relevant. The relevance of Applicants' citation of Venter et al (Science Vol.291, pages 1304-1351, 2001) is not clear. Venter's reference is about decoding and sequencing the human genome. Venter discloses that

Art Unit: 1653

only 1% of SNPs results in variation in proteins, and that the task of determining which SNPs have functional consequences remains an open challenge, (see abstract).

Therefore, since Applicants have not disclosed the physiological relevance of the claimed polynucleotides, one of ordinary skill in the art would not know how to use it.

Furthermore, the fact that the claimed nucleic acid encodes a sequence and can be used to identify how exons that are actually spliced together to produce active transcript, does not provide the claimed nucleic acid a specific and substantial utility.

The instant claims are drawn to nucleic acid molecules, not methods of specifically defining portions of a gene that actually encodes a sequence. Finally, Applicants are correct in that the assertion of one credible utility is needed to meet the requirement under 35 U.S.C. § 101, however, said utility must also be specific and substantial (real world use). The instant case fails to disclose a specific and substantial use for the claimed nucleic acid, because there is no biological significance nor correlation to a specific disease state attached to said nucleic acid.

Finally Applicants argue that the current rules and regulations regarding the examination of patent application is and always has been the patent laws as set forth in 35 U.S.C. and patent rules as set forth in 37 C.F.R., and not the manual of patent examination procedures or particular guidelines for patent examination. Furthermore, Applicants submit that it is the job of the judiciary and not the USPTO to interpret these laws and rules. Again applicants cite various new patents that were recently issued, and contend that it is capricious and arbitrary to hold the instant Applicants on a different standard.

Art Unit: 1653

This argument has been considered but is deemed unpersuasive. The Examiner is only applying and enforcing the requirements under 35 U.S.C. § 101, which requires that an invention must not only be novel but must also be useful. The contents of 35 U.S.C., 37 C.F.R., judicial decisions, and guidelines established by the USPTO are not subject to examiner review and will not be questioned or defended by the Examiner. These decisions made by legally empowered government entities to which the Examiner is subordinate and those decisions will be followed without question by the examining corps. Finally, Applicants are reminded that each Patent Application is examined on its' own merits and each Patent Application must meet the criteria set forth in the Revised Interim Utility Guidelines, for a specific and substantial credible asserted utility, or a well established utility.

Claims 1-3 and 5-7 also stands rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above and in the previous office action, one skilled in the art clearly would not know how to use the claimed invention.

Applicants argue that the claims have been shown to have specific, substantial and credible utility. Applicants' arguments have been considered but, for reasons stated above and in the previous Office Action, are not deemed to be persuasive.

Art Unit: 1653

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3 and new claims 5-7 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement for reasons of record, set forth in the office action mailed 1/28/04, pages 8-11. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

As stated in the previous office action, even in the case that the claimed polynucleotides were shown to be supported by a specific and substantial utility, the Specification does not provide support for using the claimed polynucleotides in any methods of treatment or diagnosis or methods of screening for drugs. The function of the proteins encoded by the polynucleotides of the present invention appears to have been unknown at the time of the invention and using the claimed polynucleotides to produce the protein for use in any method of treatment, drug screening, or diagnosis would have required characterization of the role and relationship of the encoded protein to any diseases or disorders.

Applicants argue that uses of the claimed invention do not require knowledge of any functional aspects of the amino acid sequence and that the nucleic acid molecules could be used in gene expression analysis and chromosomal mapping. Thus, it

Art Unit: 1653

appears that Applicants agree with the examiners rejection concerning lack of enablement for uses that involve knowledge of the protein function and its relationship with any disease. However, the examiner notes that claims 2-3, and 5-7 comprise a cDNA molecule that *encodes the amino acid sequence* of SEQ ID NO:4 and recombinant *expression* vectors and host cells that encompass the nucleotide sequence. Therefore, the intended use of these claims is in expressing the encoded protein. However, for the reasons cited in the previous office action and in the utility rejection above, enablement of this intended use is not supported by the specification because the function and utility of the product (the encoded protein) of this intended use was not known at the time of filing the present application.

With respect to Applicants arguments concerning using the cDNA for gene expression analysis, chromosomal mapping, PCR based screening and detection methods, determination of tissue expression patterns, in situ hybridization, and large scale nucleic acid screening techniques, these methods have been addressed in the utility and enablement rejection above. Since the claims are not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth in the rejection under 35 U.S.C. 101 above and in the previous office action, one skilled in the art clearly would not know how to use the claimed invention.

Conclusions

No Claims are allowable.

Art Unit: 1653


THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

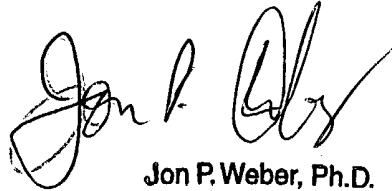
A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Holly Schnizer whose telephone number is (571) 272-0958. The examiner can normally be reached on Monday through Wednesday from 8 am to 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on (571) 272-0925. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


Holly Schnizer
August 24, 2004


Jon P. Weber, Ph.D.
Primary Examiner